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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,330	12/31/2001	Shmuel Ben-Sasson	BEN-SASSON=7	6244

1444 7590 07/25/2003

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 07/25/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,330	BEN-SASSON, SHMUEL	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2003 and 16 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37,39,41-45,47,49-52,54-57 and 59-66* is/are pending in the application.

4a) Of the above claim(s) *7-11 and 14-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12,13,22,24,26-37,39,41-45,47,49-52,54-57 and 59-66* is/are rejected.

7)☒ Claim(s) *23 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claims 7-11 and 14-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper Nos. 8 and 10.

2. It is noted that the declaration filed April 5, 2002 refers to U.S. Application Serial No. 09/458,491 in the section claiming benefit under 35 U.S.C. 120. However, this application is not cited either in the application data sheet or in the first sentence of the specification. Should Applicant wish to include this application in any claim for priority, Applicant will have to submit an amendment to their current claim for priority and in addition submit a petition under 37 CFR 1.78.

3. The drawings are objected to because in Figure 3A, "Untreated" is misspelled. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

4. The disclosure is objected to because of the following informalities: The priority claim at page 1, lines 3-9, is objected to because the serial number of the parent PCT application is incorrect. The correct serial number is PCT/US00/32852. Also, the status of the parent U.S. patent application needs to be updated. At page 1, line 15, "phosphorylate" is misspelled. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 3, line 9. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The status of the U.S. Patent applications cited in the specification, e.g., at page 3, lines 13 and 14; page 4, line 5; page 5, line 11; page 6, line 1; and page 7, line 1; must be updated. At page 8, line 9, "molecule

compounds" should be two words. At page 15, lines 2, 3, and 5, and at page 24, line 8, the meaning of the box after "TGF" is not clear. It may be that the Greek letter β was intended. The meaning of paragraph [0042] is uncertain. It is believed that if "up to 20% of the amino [acid residues - sic] have been deleted", then it should be that at least 80%, not at least 20%, are maintained. SEQ ID NOS need to be inserted after the amino acid sequences at page 24, lines 11 and 12. Also, with respect to Figure 12, SEQ ID NOS need to be inserted for every amino acid sequence subject to the sequence disclosure rules, most preferably in the Brief Description of Figure 12. See 37 CFR 1.821(d). At page 42, line 20, "groups" should be changed to "group". At page 44, line 4, "trifluoromethyl-" is misspelled. At page 44, line 23 - page 45, line 1, is an incomplete sentence. Also, within this sentence, "Adamantane", "naphthalene", "toluene", and "nitrobenzoyl" are misspelled. At page 46, line 2, "myristoyl" is misspelled. At page 47, line 19, "per" should be changed to "mer". At page 54, line 12, "citrulline" is misspelled. At page 58, line 13, "cyclohexylmethyl" is misspelled. At page 81, line 4, "cirrhosis" (both occurrences) is misspelled. At page 82, line 12, "keratinocytes" is misspelled. The above grammatical and spelling errors are merely exemplary. Because of the number of changes that will need to be made to the specification, Applicant is required to make the changes through submission of a substitute specification, including the submission of a marked-up copy of the substitute specification and a statement of no new matter. See 37 CFR 1.125. Only the specification, and not the drawings, abstract, or claims, should be included in the substitute specification. Appropriate correction is required.

5. Claims 42, 45, 47, 49-52, 59-62, 64, and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. Claim 42 is dependent upon canceled claim 40. The preamble to claim 45 is unclear because it indicates that the compound comprises a series of method steps. It may be that Applicant was attempting to claim the compound in product-by-process format. Claim 45 is indefinite because in section (II) it requires that a compound be selected in section (III) which has not yet occurred. Claim 47 is unclear as to which step (i) is being referred.

6. Claims 39, 45, 47, 49-52, 54-57, 59-62, and 64-66 are objected to because of the following informalities: At claim 39, page 15 of the amendment filed April 7, 2003, line 12, and claim 47, page 22, line 18, "shorter" is misspelled. Claim 45 is not in single sentence format. Note the period at page 20, last line, of the amendment. In claim 45, under section (I), there are two sections designated (i) - see page 20, last paragraph, and page 21, second paragraph, of the amendment. Appropriate correction is required.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 37, 39, 41-45, 47, 49-52, 54-57, and 59-62 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 8, 16, 23, 24, 46-48, 63, 68-76, 85, and 86 of copending Application No. 10/038,612.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '612 application anticipate the instant claims. Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 37, 39, 45, and 47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,174,993. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '993 patent anticipate the instant claims. Note, e.g., that the claimed peptide of SEQ ID NO:15 of the '993 patent comprises a subsequence GRPPF, which has four of five amino acids in common with the partial sequence YRPPF of Applicants' HJ-loop peptide having SEQ ID NOS:3 and 10. Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

10. The effective filing date of claims 1-6, 12, 13, 22-37, 39, 41-45, 47, 49-52, 54-57, and 59-66 is deemed to be December 31, 2001, the filing date of the instant application. Claims 1-6, 12, 133, 22-37, 39, 41-45, 47, 49-52, 54-57, and 59-66 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing dates of parent applications 09/161,094 or PCT/US00/32852 because the parent applications, under the test of 35 U.S.C. 112, first

paragraph, do not disclose all of the instant claimed subject matter, e.g., do not disclose peptides based upon the HJ loop of TGFβ superfamily Ser/Thr kinase receptor. The disclosure of 09/161,094 is limited to peptides based upon the αD region of protein kinases, and the disclosure of PCT/US00/32852 is limited to peptides based upon the B4-5 region of protein kinases.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 37, 39, 45, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Holmes (U.S. Patent No. 5,527,681). Holmes teaches the linear peptide of SEQ ID NO:25 consisting of the sequence FLRRQ, acetylated on its amino terminus, and linked by an amide bond at its carboxyl terminus to a solid phase surface. See column 25, Table 2. This peptide has four of five residues the same as the partial sequence FLQRQ in Applicant's αD sequences having SEQ ID NOS:1 and 2 (see page 72, Table 1). Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

13. Claims 1, 2, 12, 13, 26, 31, 37, 39, 41, 43-45, 47, 49, 51, 52, 54, 56, 57, 59, and 61-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al (U.s. Patent No. 5,340,800).

Liu et al teach peptides at claim 9 comprising the subsequence TANML. The peptides are used therapeutically in the form of pharmaceutical compositions to treat diseases involving an inflammatory response to an infection (see, e.g., the Abstract and column 6, lines 18-32). This subsequence has three of five residues in common with the reverse of the partial sequence LKCAT in Applicant's αD sequences having SEQ ID NOS:19 and 20 (see page 72, Table 1). Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art. Diseases involving an inflammatory response to an infection constitute diseases involving an immune related response, and therefore Liu et al's therapeutic method meets Applicant's requirement for a method for the modulation of tissue-remodeling.

14. Claims 1, 2, 12, 13, 26, 31, 37, 39, 41, 43-45, 47, 49, 51, 52, 54, 56, 57, 59, and 61-67 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 96/32411. The WO Patent Application '411 teaches peptides comprising SEQ ID NOS:8 (which comprises QNSSE), 34 (which comprises NNSSE), and 37 (which comprises DNSSE). The peptides are also administered to patients to treat proliferative cell disorders, such as arteriosclerosis, inflammatory joint disease, psoriasis, and cancer. See, e.g., page 7, lines 14-24, and claims 6 and 18-21. These subsequences have three of five residues in common with the partial sequence RNSST in Applicants' B4-B5 sequences having SEQ ID NOS:11 (see page 72, Table 1). Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

Treatment of diseases involving proliferative cell disorders, such as arteriosclerosis, inflammatory joint disease, psoriasis, and cancer meets Applicant's requirement for a method for the modulation of tissue-remodeling.

15. Claims 1, 2, 12, 13, 26-28, 31-33, 37, 39, 41, 43-45, 47, 49, 51, 52, 54, 56, 57, 59, and 61-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Stuber et al (U.S. Patent No. 5,478,810). Stuber et al teach the linear peptides GPRPP-NH_2, GPRPPR-NH_2, and GPRPPP-NH(isopropyl). The peptides are administered in vivo to inhibit fibrin-thrombin clotting. In general, modification with an alkyl chain having up to four carbon atoms is taught. See column 1, lines 59-60; column 2, lines 12-13, 17-18, 20, and 24-25; and the claims. For example, the peptide GPRPPP-NH(isopropyl) is modified at the C-terminus with an isopropyl group, comprises a subsequence PRPPP which has three of five residues in common with the partial sequence YRPPF in Applicant's JH-loop sequence having SEQ ID NOS:3 and 10, and comprises a subsequence GPRPP which has three of five residues in common with the partial sequence DYRPP in Applicant's JH-loop sequence having SEQ ID NO:4. Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art. Inhibiting fibrin-thrombin clotting constitutes modulating scarring, wound healing, and prevention of adhesion formation, and therefore meets Applicant's requirement for a method for the modulation of tissue-remodeling.

16. Claims 1-4, 12, 13, 26-37, 39, 41, 43-45, 47, 49, 51, 52, 54, 56, 57, 59, and 61-67 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 98/53050. The WO Patent Application '050 teaches treating diseases such as cancer, inflammatory

diseases, and autoimmune diseases, by administering peptide derivatives of the HJ loop of a serine/threonine kinase. The peptides can be modified at their N- and/or C-terminus, e.g., with myristyl-Gly groups. Specific peptides are shown in Figure 4 and especially in Figure 6A, in which peptide K098H101 corresponds to Applicant's elected SEQ ID NO:21. See, e.g., the Abstract; page 3, lines 19-25; page 7, lines 15-23; page 16, line 26 - page 17, line 2; page 21, line 32 - page 26, line 29; Example 3; and Figures 4 and 6A. Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

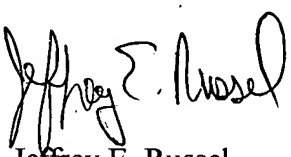
17. Claims 1, 5, 6, 12, 13, 26, 27, 29-32, 34-37, 39, 41, 43-45, 47, 49, 51, 52, 54, 56, 57, 59, and 61-67 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 98/53051. The WO Patent Application '051 teaches treating osteoporosis by administering peptide derivatives which inhibit Src activity or which activate Csk (see, e.g., page 4, lines 11-18; page 24, lines 16-20; and page 26, lines 19-25). As peptide derivatives of Src, the WO Patent Application '051 teaches HJ11, HJ11.1, and HJ8 (see Table 1 at pages 35-36, and Figure 3A), which comprise a subsequence VPFPG which has three of five residues in common with the partial sequence DLFPG in the HJ-loop sequence of BMR2 (see Applicant's Figure 12). HJ11 comprises a hydrophobic moiety, acetyl, attached through a glycine residue to the N-terminus of the peptide. Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

18. Claims 1, 2, 5, 6, 12, 13, 22, 24, 26, 31, 37, 39, 41-45, 47, 49-52, 54-57, and 59-67 are rejected under 35 U.S.C. 102(e) as being anticipated by Khosla et al (U.S. Patent No. 6,548,482) in view of Ballard et al (U.S. Patent No. 5,470,828). Khosla et al teach a method of treating osteoporosis and increasing bone mass by administering a complex of an IGFIIE polypeptide, an IGFBP2 polypeptide, and optionally a compound which can be an IGFII polypeptide or IGFI. The IGFIIE polypeptide can be $IGFIIE_{1-87}$ or $IGFIIE_{1-104}$. See, e.g., claims 5, 7-9, and 11-15. Khosla et al give the amino acid sequence for IGFIIE in SEQ ID NO:7, which comprises the partial sequence GIVEE at residues 41-45 which has five of five residues in common with the partial sequence GIVEE in the HJ-loop sequence of ALK3 (see Applicant's Figure 12). Further, Ballard et al teaches the amino acid sequences for IGF-1 (see column 1, lines 20-25) and for IGF-2 (see column 2, lines 7-13). IGF-1 comprises the partial sequence GIVDE which has four of five residues in common with the partial sequence GIVEE in the HJ-loop sequence of ALK3 (see Applicant's Figure 12), and IGF-2 comprises the partial sequence GIVEE which has five of five residues in common with the partial sequence GIVEE in the HJ-loop sequence of ALK3 (see Applicant's Figure 12). Accordingly, the compositions of Khosla et al which contain the compound which can be an IGFII polypeptide or IGFI contain two different compounds (including the IGFIIE polypeptide) which meet the sequence and functional requirements of Applicant's active agents. Note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art, and that intended use limitations do not impart patentability to product claims where the product is otherwise anticipated by the prior art.

19. Claims 23 and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and if rewritten to omit the nonelected amino acid sequences. The prior art of record does not teach or suggest administering a compound having Applicant's SEQ ID NO:21 in order to enhance bone healing or to increase bone density. The WO Patent Application 98/53050, applied above, does not teach or suggest that its compound has such therapeutic properties. Further, the WO Patent Application '050 is not deemed to anticipate these claims on the basis of inherency, because it does not teach administering its compound of SEQ ID NO:21 to a patient with an injured bone, and does not necessarily teach administering its compound of SEQ ID NO:21 to a patient in such a manner where the compound will contact bone specifically.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel
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JRussel
July 23, 2003